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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/527,028	03/16/2000	Sylvie Veriac	0198/053	1839

7590 11/05/2002

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EXAMINER

GABEL, GAILENE

ART UNIT PAPER NUMBER

1641

DATE MAILED: 11/05/2002

12

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/527,028

Applicant(s)

VERIAC ET AL.

Examiner

Gailene R. Gabel

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 18 April 2002 and 14 August 2002.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 12 and 14-25 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 12 and 14-25 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____.
- 4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 8/14/02 has been entered.

Amendment Entry

2. Applicant's amendment and response filed 4/18/02 in Paper No. 7 is acknowledged and has been entered. Claim 12 has been amended. Claim 13 has been cancelled. Claim 25 has been added. Accordingly, claims 12 and 14-25 are pending and are under examination.

Rejections Withdrawn

Claim Rejections - 35 USC § 103

3. In light of Applicant's amendment, the rejection of claims 12 and 14-25 under 35 U.S.C. 103(a) as being unpatentable over Takarada et al. (US 5,677,183) in view of Hamaguchi et al. (US 5,389,549) and in further view of Uchihashi et al. (US 5,968,832), is hereby, withdrawn.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claims 12 and 14-25 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In claim 12, preamble, "basophile" should be "basophil". Further, "hemeglobin" should be "hemoglobin".

Claim 25 has improper antecedent basis problem in reciting, "A single reagent ... according to claim 12". Also in claim 25, "basophile" should be "basophil" and "hemeglobin" should be "hemoglobin".

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claim 25 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

In this case, the specification does not appear to provide any literal support for the recitation of "nitrogenous compound comprises a quaternary ammonium

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compound". Applicant points to page 6, lines 16-17 (specifically lines 10-30) for support which discloses that the detergent is chosen from compounds such as the quaternary ammonium salts but fails to provide literal support for "nitrogenous compound comprises a quaternary ammonium compound". Further in lines 29-30, the specification provides that the nitrogenous compound is advantageously a thiourea or in particular, 1,3-dimethyl-2-thiourea, but fails to provide literal support for the recitation of "nitrogenous compound comprises a quaternary ammonium compound". Furthermore, none of the originally filed claims recited this limitation in question. Recitation of claim limitation lacking literal or adequate support in the specification or originally filed claims constitutes new matter.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to

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consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

6. Claims 12 and 14-25 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sakata et al. (US 5,538,893) in view of Hamaguchi et al. (US 5,389,549) and in further view of Uchihashi et al. (US 5,968,832) for reason of record and as follows.

Sakata et al. disclose a single reagent for analyzing and classifying leucocytes including basophil, which is capable of determining cell size and morphological features of all leucocytes (see Abstract and column 6, lines 60-64). Specifically, the single reagent comprises a buffer for adjusting the pH to 2.5 - 4.0, a cationic detergent (surfactant), and also an inorganic salt. The cationic detergent includes quaternary ammonium salts for complete lysis of erythrocytes and baring the nuclei of granulocytes other than basophil (see column 4, lines 21-59). The cationic detergent is preferred at a concentration of 1 g/l to 10 g/l (see column 4, lines 53-64). The reagent buffer used includes citric acid and tartaric acid in addition to alkali metal hydroxides such as sodium hydroxide and potassium hydroxide, for adjusting pH to a desired pH of 2.0 - 5.0 (see column 5, lines 25-40). The inorganic salts include alkali metal salts such as sodium chloride and potassium chloride (see column 6, lines 1-6). According to Sakata et al., the surfactants, the buffer, and the salts are prepared and mixed at desired ratios (see column 5, lines 44-63). Sakata et al. disclose that at appropriate concentrations, cell lysing is exhibited and lymphocytes and monocytes, immature granulocytes and basophils which include a large percentage of basophilic granules are hardly shrunk allowing differentiation in sizes of leucocytes (see column 7, lines 36-47).

Sakata et al. differ in failing to disclose the single reagent as further comprising nitrogenous compound.

Hamaguchi et al. disclose a hematologic reagent for counting and classifying leucocytes including basophil and lysing erythrocytes. Specifically, the reagent comprises a blood diluent including a phosphate buffer which maintains the pH at 1.5 - 5.0, sodium chloride, an nonionic detergent; and a nitrogenous compound for use in reducing the size of monocytes in leucocytes. Hamaguchi et al. disclose that nitrogenous compounds are solubilizing agents which include thiourea or 1,3-dimethylurea. Specifically, Hamaguchi et al. disclose that when incorporated into a reagent, the solubilizing agent selectively promotes the action of the lysing reagent into monocytes. Such selective action of solubilizing agents to monocytes is also effective with other reagents used in leucocyte classification. Hamaguchi et al. further disclose that the reagent comprising a buffer having potassium phthalate, hydrochloric acid, nitric acid, and a lysing agent at an acidic pH of 3.0, is enabled for basophil measurement.

Sakata et al. and Hamaguchi et al. differ in failing to disclose the reagent capable of additionally measuring hemoglobin content.

Uchihashi et al. disclose a reagent for measurement of leucocytes and hemoglobin concentration including a cationic detergent, a hemoglobin stabilizer such as sulfosalicylic acid, a chelating agent having a nitrogen compound, and a salt (see Abstract).

One of ordinary skill in the art at the time of the instant invention would have reasonable expectation of success in incorporating the solubilizing agent / nitrogenous

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compound as taught by Hamaguchi and the hemoglobin reagent as taught by Uchihashi into the reagent taught by Sakata because Hamaguchi specifically suggested conventional applicability of nitrogenous compounds with all other reagents used in leucocyte classification such as the reagent taught by Sakata and Uchihashi specifically taught that hemoglobin stabilizers exhibit applicability in hematologic reagents by binding to the heme of methemoglobin denatured with cationic surfactants.

Sakata et al., Hamaguchi et al., and Uchihashi et al. differ in failing to disclose the specific concentration parameters of elements recited in claims 23 and 24.

It is, however, maintained that the concentration parameters such as detergent [0.2-20 g/l] and nitrogenous compound [0.1-10 g/l] recited in claim 23 and potassium chloride [5-15 g/l], 1,3- dimethyl-2- thiourea [0.5-5 g/l], dodecyltrimethylammonium chloride [0.5-5 g/l], and potassium hydrogen phosphate / HCl [1.0-10 g/l] which are recited in claim 24, are all result effective variables which the prior art references have shown may be altered in order to achieve optimum results. It has long been settled to be no more than routine experimentation for one of ordinary skill in the art to discover an optimum value of a result effective variable. "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum of workable ranges by routine experimentation." Application of Aller, 220 F.2d 454, 456, 105 USPQ 233, 235-236 (C.C.P.A. 1955). "No invention is involved in discovering optimum ranges of a process by routine experimentation." Id. at 458, 105 USPQ at 236-237. The "discovery of an optimum value of a result effective variable in a known process is ordinarily within the skill of the art." Application of Boesch, 617 F.2d 272, 276,

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205 USPQ 215, 218-219 (C.C.P.A. 1980). Since Applicant has not disclosed that the specific limitations recited in instant claims 23 and 24 are for any particular purpose or solve any stated problem and the prior art teaches that the different reagent elements and parameters often vary according to the reagent system used or sample being analyzed and parameters appear to work equally as well; absent unexpected results, it would have been obvious for one of ordinary skill to discover the optimum workable ranges of the methods disclosed by the Sakata, Hamaguchi, and Uchihashi by normal optimization procedures known in the leucocyte differentiation art.

Response to Arguments

7. Applicant's arguments filed 4/18/02 have been fully considered but they are not persuasive.

A) Applicant argues that Sakata fails to differentially distinguish each of the five classes of leucocytes, i.e. neutrophils are not distinguished from eosinophils and lymphocytes are not distinguished from monocytes.

In response, it is noted that the features upon which Applicant relies (i.e., reagent allows differentially distinguishing between each of the five classes of leucocytes, i.e. neutrophils are distinguished from eosinophils and lymphocytes are distinguished from monocytes) are not recited in the rejected claims. Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). Additionally, the combined teaching of Sakata which teaches a reagent comprising a citric acid or

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tartaric acid buffers, a cationic reagent, and alkali metal salts, Hamaguchi which teaches incorporating nitrogenous compounds into leucocyte classification reagents for monocyte identification, and Uchihashi which teaches incorporating hemoglobin stabilizers into leucocyte classification reagents for measuring hemoglobin, suggests a capacity to perform leucocytic differentiation function in addition to hemoglobin measure by virtue of the presence of all required elements in performing the desired and required function.

B) Applicant argues that Hamaguchi teaches away from the claimed invention in disclosing inoperability; thus, exclusion of quaternary ammonium salts, in his reagent.

In response to applicant's argument that the teaching of quaternary ammonium salts in the teaching of Sakata renders the combination between the Sakata reference and Hamaguchi reference inoperable, the test for obviousness is not whether the features of a secondary reference may be bodily incorporated into the structure of the primary reference; nor is it that the claimed invention must be expressly suggested in any one or all of the references. Rather, the test is what the combined teachings of the references would have suggested to those of ordinary skill in the art. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981). In this case, Sakata discloses a single reagent for analyzing and classifying leucocytes including basophil, which comprises a buffer for adjusting the pH to 2.5 - 4.0, a cationic detergent, and also an inorganic salt. The cationic detergent includes quaternary ammonium salts for complete lysis of erythrocytes and baring the nuclei of granulocytes other than basophil. Hamaguchi is

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incorporated for his disclosure of a hematologic reagent for counting and classifying leucocytes including basophil and lysing erythrocytes, which comprises a phosphate buffer which maintains the pH at 1.5 - 5.0, sodium chloride, an nonionic detergent; and a nitrogenous compound, i.e. thiourea or 1,3- dimethylurea, which selectively promotes the action of the lysing reagent into monocytes for use in reducing the size of monocytes in leucocytes. According to Hamaguchi, the selective action of solubilizing agents to monocytes is also effective for use with other reagents capable of leucocyte classification; thus, suggesting applicability of nitrogenous compounds with other reagents such as taught by Sakata.

C) Applicant argues that Hamaguchi in further combination with Uchihashi, also teaches away from the claimed invention in disclosing inoperability; thus, exclusion of quaternary ammonium salts, in their reagents.

In response to applicant's argument that the teaching of quaternary ammonium salts in the teaching of Sakata renders the combination between the Sakata reference and the Hamaguchi and Uchihashi reference inoperable, the test for obviousness is not whether the features of a secondary reference may be bodily incorporated into the structure of the primary reference; nor is it that the claimed invention must be expressly suggested in any one or all of the references. Rather, the test is what the combined teachings of the references would have suggested to those of ordinary skill in the art. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981). In this case, Sakata discloses a single reagent for analyzing and classifying leucocytes including basophil,

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which comprises a buffer for adjusting the pH to 2.5 - 4.0, a cationic detergent, and also an inorganic salt. The cationic detergent includes quaternary ammonium salts for complete lysis of erythrocytes and baring the nuclei of granulocytes other than basophil. Hamaguchi is incorporated for his disclosure of a hematologic reagent for counting and classifying leucocytes including basophil and lysing erythrocytes, which comprises a phosphate buffer which maintains the pH at 1.5 - 5.0, sodium chloride, a nonionic detergent; and a nitrogenous compound, i.e. thiourea or 1,3- dimethylurea, which selectively promotes the action of the lysing reagent into monocytes for use in reducing the size of monocytes in leucocytes. According to Hamaguchi, the selective action of solubilizing agents to monocytes is also effective for use with other reagents capable of leucocyte classification; thus, suggesting applicability of nitrogenous compounds with other reagents such as taught by Sakata. Sakata et al. and Hamaguchi et al. differ in failing to disclose the reagent capable of additionally measuring hemoglobin content. Uchihashi is further incorporated with the combination of Sakata and Hamaguchi, only for the disclosure of a hemoglobin stabilizer such as sulfosalicylic acid, for measuring the hemoglobin, in addition to cationic detergent, a chelating agent having a nitrogen compound, and a salt, combined in a reagent for measurement of leucocytes and hemoglobin concentration. One of ordinary skill in the art at the time of the instant invention would have reasonable expectation of success in incorporating the solubilizing agent / nitrogenous compound as taught by Hamaguchi and the hemoglobin reagent as taught by Uchihashi into the reagent taught by Sakata because Hamaguchi specifically suggested conventional applicability of nitrogenous compounds with all other reagents

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used in leucocyte classification such as the reagent taught by Sakata and Uchihashi specifically taught that hemoglobin stabilizers exhibit applicability in hematologic reagents by binding to the heme of methemoglobin denatured with cationic surfactants.

8. No claims are allowed.

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gailene R. Gabel whose telephone number is (703) 305-0807. The examiner can normally be reached on Monday-Thursday from 6:30 AM - 4:00 PM and alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le can be reached on (703) 308-3399. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4242 for regular communications and (703) 308-4242 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Gailene R. Gabel
Patent Examiner
Art Unit 1641
November 2, 2002

gg

Christopher L. Chin

CHRISTOPHER L. CHIN
PRIMARY EXAMINER
GROUP 1800/69/